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(FILE 'HOME' ENTERED AT 11:56:07 ON 06 MAY 2005)

FILE 'REGISTRY' ENTERED AT 11:56:15 ON 06 MAY 2005
E NORKETOTIFEN/CN
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 11:57:15 ON 06 MAY 2005
L2 20 S L1
L3 13 S L2 AND PREP/RL

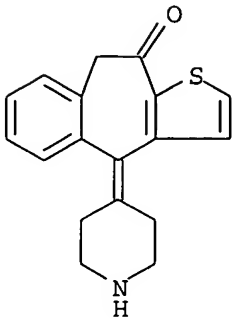
=> s l2 not l3
L4 7 L2 NOT L3

=> d 1-7 bib abs hitstr

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:1006787 CAPLUS
DN 140:47532
TI Quaternary ammonium cyclodextrins as pharmaceutical penetration enhancers
IN Kis, Georg Ludwig; Schoch, Christian; Szejtli, Jozsef
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003105867	A1	20031224	WO 2003-EP6192	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
	RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	BR 2003011722	A	20050301	BR 2003-11722	20030612
	EP 1515729	A1	20050323	EP 2003-740232	20030612
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	EP 2002-13074	A	20020613		
	EP 2002-28554	A	20021220		
	WO 2003-EP6192	W	20030612		

OS MARPAT 140:47532
AB The use of quaternized ammonium cyclodextrin compds. in the preparation of an anti-infective pharmaceutical as preservative and penetration enhancer is disclosed. Thus, a thin-layer film composition contained Mowiol 26-88 100, HPC 40, quaternary ammonium β-cyclodextrin derivative 50, and glycerin 10 mg.
IT **34580-20-6**, NorKetotifen
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quaternary ammonium cyclodextrins as pharmaceutical penetration enhancers)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



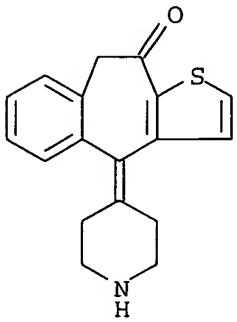
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:7824 CAPLUS
DN 130:57237
TI Compounds with combined antihistaminic and mast cell stabilizing activities, intended for ophthalmic use
IN Aberg, A. K. Gunnar
PA Bridge Pharma, Inc., USA
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9856381	A1	19981217	WO 1998-US12031	19980609
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9878336	A1	19981230	AU 1998-78336	19980609
	EP 1014979	A1	20000705	EP 1998-926517	19980609
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6207684	B1	20010327	US 1999-445118	19991202
PRAI	US 1997-49103P	P	19970609		
	WO 1998-US12031	W	19980609		

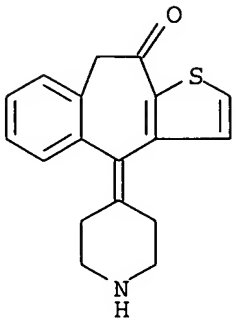
AB The compds. norketotifen [10-oxo-4H-benzo[4,5] cyclohepta[1,2-b]thiophene] and 10-hydroxynorketotifen and their salts have potent ocular antihistaminic and anti-inflammatory properties. The compds. have minimal irritating effects in the eye and have ophthalmic usefulness. Thus, tablets contained norketotifen 2, microcryst. cellulose 30, lactose 70, calcium stearate 2, and FD&C Blue #1 Lake 0.03 mg/tablet.
IT **34580-20-6**, Norketotifen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(pharmaceuticals with combined antihistaminic and mast cell stabilizing activities for ophthalmic use)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:131229 CAPLUS
DN 106:131229
TI Species differences in metabolism of ketotifen in rat, rabbit and man: demonstration of similar pathways in vivo and in cultured hepatocytes
AU Le Bigot, J. F.; Begue, J. M.; Kiechel, J. R.; Guillouzo, A.
CS Cent. Rech. Pharm., Sandoz S.a r.l., Rueil-Malmaison, 92505, Fr.
SO Life Sciences (1987), 40(9), 883-90
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB In vitro drug metabolism by cultured rat, rabbit and human adult hepatocytes has been studied, using ketotifen (ZADITEN) [34580-13-7] as a model substrate because it is biotransformed in vivo by various metabolic pathways in man and animals. The major in vivo pathways were demonstrated in vitro, namely oxidation in rat hepatocytes, oxidation, glucuronidation and sulfation in rabbit hepatocytes, reduction and glucuronidation in human hepatocytes. Human hepatocytes were the most stable in culture, displaying ketotifen biotransformation for at least 1 wk. These results clearly demonstrated that cultured hepatocytes retain their in vivo specific drug metabolizing activities, including inter-species polymorphism, for a few days. Therefore, pure hepatocyte cultures represent a useful system suitable for drug metabolism studies.
IT **34580-20-6**
RL: BIOL (Biological study)
(ketotifen metabolite in hepatocyte of humans and laboratory animals)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

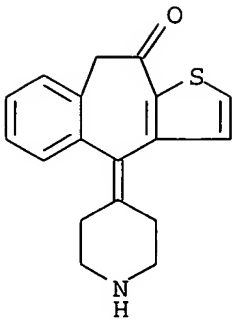


L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1985:467897 CAPLUS
DN 103:67897
TI Human hepatocyte cultures and their use
IN Guguen, Christiane; Guillouzo, Epouse; Guillouzo, Andre; Bourel, Michel
PA Institut National de la Sante et de la Recherche Medicale (INSERM), Fr.
SO Fr. Demande, 34 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

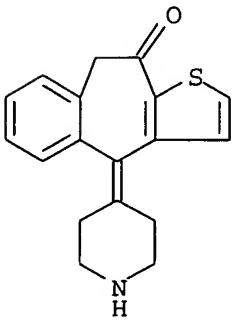
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2545100	A1	19841102	FR 1983-7148	19830429
	FR 2545100	B1	19851220		
	US 5112757	A	19920512	US 1987-34983	19870406
PRAI	FR 1983-7148	A	19830429		
	US 1984-694518	B1	19841227		

AB A method is described for the long-term culture of human hepatocytes (adult or fetal) which maintain their functional integrity and for the use of these cultures in biochem. and biol., especially as models for studying hepatic function in pharmacol. and pathol. Thus, hepatocytes were cocultured with liver epithelial cells (transformed or nontransformed) of animal, especially rat, origin, in the presence of pork insulin and bovine serum albumin in serum-containing medium, addition of hydrocortisone hemisuccinate after 24-30 h, and separation of the hepatocytes by incubation with collagenase in Ca-free medium. After approx. 24 h following confluence of the cells, reticuline fibers appear. An extracellular heterogeneous material appearing in the culture contains collagen and fibronectin. The hepatocytes retain their specific functions for at least 6-8 wks. Examples are also given of the use of the hepatocyte cultures for studying the breakdown of ketotifene to its metabolites and for the production of viral antigens.

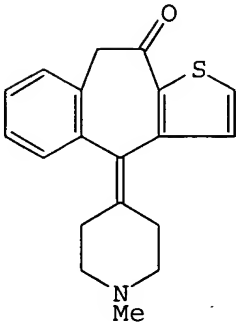
IT **34580-20-6**
RL: ANST (Analytical study)
(in cultured human hepatocytes, ketotifene metabolism in relation to)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1984:44820 CAPLUS
DN 100:44820
TI Metabolism of ketotifen by human liver microsomes. In vitro characterization of a tertiary amine glucuronidation
AU Le Bigot, Jean F.; Cresteil, Thierry; Kiechel, Jean R.; Beaune, Philippe
CS Cent. Rech. Pharmacocinet., Lab. Sandoz S.a r.l., Rueil-Malmaison, 92506, Fr.
SO Drug Metabolism and Disposition (1983), 11(6), 585-9
CODEN: DMDSAI; ISSN: 0090-9556
DT Journal
LA English
AB Biotransformation of ketotifen [34580-13-7] was investigated in vitro using human liver microsomes. Three of the 4 metabolic pathways observed in vivo in man were exhibited under the conditions of incubation, namely demethylation, N-oxidation, and N-glucuronidation. Ketoredn., which probably has a cytosolic localization, was not observed The kinetic parameters of the N-glucuronidation (KM for ketotifen and UDPGA, and Vmax) were determined with native and detergent-treated microsomes. Treatment by Triton X-100 increased by about 3-fold the conjugation reaction. No sex difference was observed and N-glucuronidation did not seem to be inhibited either by bilirubin or by 4-nitrophenol.
IT **34580-20-6**
RL: BIOL (Biological study)
(ketotifen metabolite, formation of, by human liver microsome)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

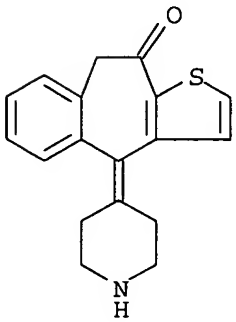


L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1982:192893 CAPLUS
DN 96:192893
TI Metabolism and pharmacokinetics of ketotifen in children
AU Kennedy, G. R.
CS Wander Pharm., Feltham, UK
SO Research and Clinical Forums (1982), 4(1), 17-20
CODEN: RCLFD4; ISSN: 0143-3083
DT Journal
LA English
GI



I

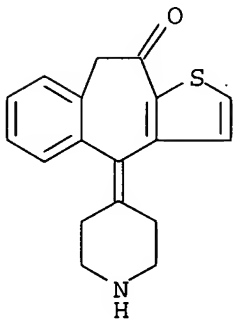
AB Metabolic and pharmacokinetic data on ketoifen (I) [34580-13-7] in adults and children are presented supporting the concept that a higher dose of ketotifen is necessary in children in order to obtain beneficial effect.
IT **34580-20-6**
RL: BIOL (Biological study)
(as ketotifen metabolite, in human)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1982:28187 CAPLUS

10069663

DN 96:28187
TI Application of capillary column gas chromatography to the elucidation of the metabolism of ketotifen in the monkey and man
AU Guerret, M.; Julien-Larose, C.; Lavene, D.
CS Cent. Rech. Pharmacocinet., Lab. Sandoz, Rueil-Malmaison, 92506, Fr.
SO C.-R. - Congr. Eur. Biopharm. Pharmacocinet., 1st (1981), Volume 2, 317-21. Editor(s): Aiache, J. M.; Hirtz, J. Publisher: Tech. Documentation, Paris, Fr.
CODEN: 46QKA2
DT Conference
LA French
AB Capillary column gas chromatog. was used to determine ketotifen (I) [34580-13-7] and its metabolites in the plasma and urine of rhesus monkeys, baboons, gibbons, chimpanzees, and humans after oral administration of I. In addition to unchanged I, 6 metabolites were found in all species: I N-glucuronide [79987-40-9], 10-hydroxyketotifen [43076-12-6] and its N-glucuronide [79994-31-3], norketotifen [**34580-20-6**], and 10-hydroxynorketotifen [79987-41-0] and its N-glucuronide [79987-39-6]. The quant. proportions of these metabolites varied from species to species. In man, the major urinary products were I glucuronide and 10-hydroxyketotifen glucuronide. About 65% of the I dose was excreted in human urine (as unchanged I plus metabolites).
IT **34580-20-6**
RL: FORM (Formation, nonpreparative)
(formation of, as ketotifen metabolite, species in relation to)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



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FILE 'REGISTRY' ENTERED AT 11:56:15 ON 06 MAY 2005
E NORKETOTIFEN/CN
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 11:57:15 ON 06 MAY 2005
L2 20 S L1
L3 13 S L2 AND PREP/RL

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L1 1 NORKETOTIFEN/CN

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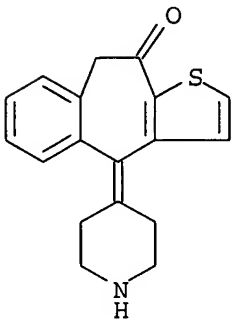
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 34580-20-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Norketotifen**
FS 3D CONCORD
MF C18 H17 N O S
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20 REFERENCES IN FILE CA (1907 TO DATE)
20 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10069663

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L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:208107 CAPLUS
DN 134:242680
TI Optically active isomers of ketotifen and therapeutically active metabolites thereof
IN Aberg, A. K. Gunnar; Wright, George E.; Chen, Jan L.; Maioli, Andrew T.
PA Bridge Pharma, Inc., USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001019367	A1	20010322	WO 2000-US24892	20000912
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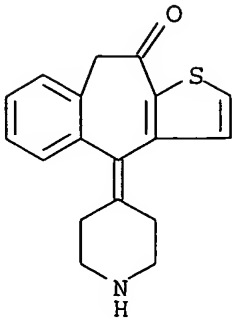
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2383222	AA	20010322	CA 2000-2383222	20000912
	BR 2000013935	A	20020514	BR 2000-13935	20000912
	EP 1218007	A1	20020703	EP 2000-966709	20000912
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003509369	T2	20030311	JP 2001-523001	20000912
PRAI	US 1999-153566P	P	19990913		
	US 2000-197363P	P	20000415		
	US 2000-197905P	P	20000415		
	US 2000-197906P	P	20000415		
	US 2000-197985P	P	20000415		
	WO 2000-US24892	W	20000912		

OS MARPAT 134:242680
AB Racemic norketotifen, 10-hydroxy-ketotifen, or 10-hydroxy-nor-ketotifen, and optically active isomers of ketotifen, norketotifen, 10-hydroxy-ketotifen and 10-hydroxy-norketotifen were found to have antiallergic and anti-inflammatory effects while being devoid of the severe dose-limiting sedative side effects of ketotifen. Preparation of R and S isomers of norketotifen as well as their fumarates was presented.
IT **34580-20-6**, Norketotifen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiallergic and anti-inflammatory effects of optically active isomers of ketotifen and therapeutically active metabolites)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:682123 CAPLUS
DN 129:298411
TI Benzocycloheptathiophene compounds for antihistaminics and antiasthmatics and prevention of smooth muscle hyperreactivity
IN Aberg, A. K. Gunnar; Wright, George E.; Chen, Jan L.
PA Bridge Pharma, Inc., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9843640	A1	19981008	WO 1998-US6576	19980402
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2283663	AA	19981008	CA 1998-2283663	19980402
	AU 9868812	A1	19981022	AU 1998-68812	19980402
	AU 733325	B2	20010510		
	EP 977568	A1	20000209	EP 1998-914461	19980402
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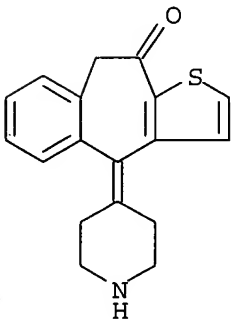
	BR 9807911	A	20000222	BR 1998-7911	19980402
	JP 2001519789	T2	20011023	JP 1998-542018	19980402
	NZ 337843	A	20011130	NZ 1998-337843	19980402
	RU 2193557	C2	20021127	RU 1999-123048	19980402
	CN 1128789	B	20031126	CN 1998-805506	19980402
	IL 131999	A1	20040620	IL 1998-131999	19980402
	MX 9908997	A	20000731	MX 1999-8997	19990930
	NO 9904823	A	19991007	NO 1999-4823	19991004
	NO 311934	B1	20020218		
	US 6207683	B1	20010327	US 1999-381351	19991029
	HK 1027961	A1	20040820	HK 2000-107262	20001115
PRAI	US 1997-43905P	P	19970403		

WO 1998-US6576 W 19980402
OS MARPAT 129:298411
AB Disclosed are N-substituted hydroxyalkyl or carboxyalkyloxyalkyl analogs of 9- and/or 10-oxo-4H-benzo[4,5]cyclohepta[1,2-b]thiophene compds., or 9-OH and/or 10-OH-substituted analogs thereof, which possess antihistaminic and antiasthmatic properties with reduced sedative side effects. The optically active isomers and the pharmaceutically acceptable salts thereof are also described. The compds. were also found to prevent smooth muscle hyperreactivity.
IT **34580-20-6**, Norketotifen
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzocycloheptathiophene compds. for antihistaminics and antiasthmatics and prevention of smooth muscle hyperreactivity, preparation, pharmaceutical compns., and use with other agents)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

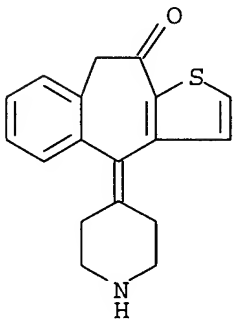


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:603313 CAPLUS
DN 119:203313
TI Preparation of dibenzocycloheptanylidenepiperidylalkoxybenzoic acid analogs as antihistaminic and allergy inhibitors
IN Kumagai, Kazuhiro; Nagasawa, Masaaki; Takahashi, Hidenori; Abe, Tooru; Omata, Takeshi; Segawa, Yoshihide
PA Zeria Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9313068	A1	19930708	WO 1992-JP1640	19921216
	W: AU, CA, JP, KR, RU, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9331707	A1	19930728	AU 1993-31707	19921216
PRAI	JP 1991-356615	A	19911225		

WO 1992-JP1640 A 19921216
OS MARPAT 119:203313
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; R = H, halo; X = CH2-CH2, CH:CH, CH2-CO-; A = benzene ring, thiophene ring, pyridine ring; B = OH, alkoxy, 1H-tetrazol-5-yl; m = 2-5 integer] are prepared K2CO3 was added to a mixture of 4-(5H-dibenzo[a,d]cyclohepten-5-ylidene)piperidine and Me 2-(2-bromoethoxy)benzoate in acetone and the resulting mixture was heated (temperature not specified) for 3 h to give I [A = benzene ring, R = H, m = 2, B = MeO, X = CH:CH]. 2-[2-[4-(10-Oxo-9,10-dihydro-4H-benzo[4,5]cyclohepta[1,2-b]thiophene-11-ylidene)-1-piperidinyl]ethoxy]benzoic acid Me ester (also prepared) had an IC50 of 1.26 μM against the effect of histamine on isolated marmot ileum. Some pharmaceutical compns. containing I are described.
IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of antihistaminics and antiallergics)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



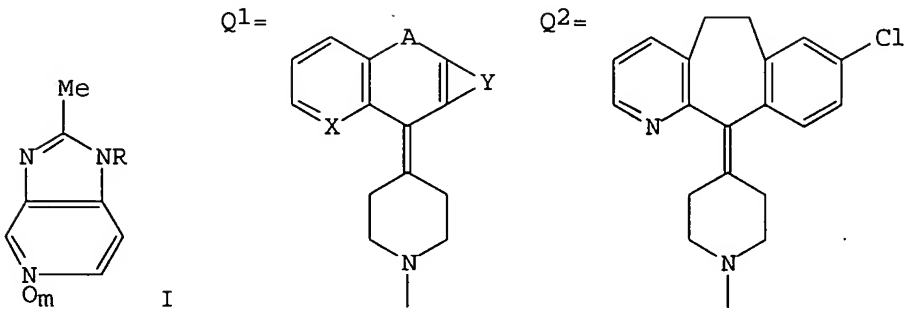
L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:22232 CAPLUS
DN 118:22232
TI Preparation of 4-benzocyloheptapynidylidene-1-(imidazopyridylbenzoyl)piperidines and analogs as antiallergics
IN Alker, David; Bass, Robert John; Cooper, Kelvin
PA Pfizer Ltd., UK; Pfizer Inc.
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214734	A1	19920903	WO 1992-EP163	19920124
	W: AU, BR, CA, FI, HU, JP, KR, NO, PL, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	CA 2099381	AA	19920814	CA 1992-2099381	19920124
	CA 2099381	C	19960709		
	AU 9211683	A1	19920915	AU 1992-11683	19920124

	AU 650322	B2	19940616		
	EP 572425	A1	19931208	EP 1992-902889	19920124
	EP 572425	B1	19940803		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	BR 9205615	A	19940517	BR 1992-5615	19920124
	JP 06504992	T2	19940609	JP 1992-503504	19920124
	JP 2506541	B2	19960612		
	HU 65947	A2	19940829	HU 1993-2327	19920124
	ES 2059212	T3	19941101	ES 1992-902889	19920124
	PL 169304	B1	19960628	PL 1992-300296	19920124
	RU 2114845	C1	19980710	RU 1993-54165	19920124
	IL 100887	A1	19960119	IL 1992-100887	19920206
	ZA 9201005	A	19930812	ZA 1992-1005	19920212
	CZ 280504	B6	19960214	CZ 1992-425	19920212
	CN 1064275	A	19920909	CN 1992-100974	19920213
	CN 1040326	B	19981021		
	US 5358953	A	19941025	US 1993-87736	19930712
	KR 9705302	B1	19970415	KR 1993-72352	19930807
	NO 9302889	A	19930813	NO 1993-2889	19930813
	NO 300592	B1	19970623		
	FI 9703558	A	19970829	FI 1997-3558	19970829
	FI 101225	B1	19980515		
PRAI	GB 1991-2997	A	19910213		
	WO 1992-EP163	A	19920124		
	FI 1993-3531	A3	19930810		

OS MARPAT 118:22232

GI



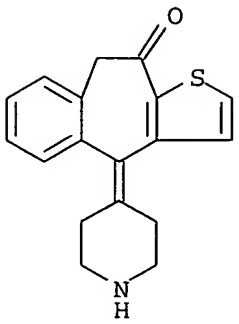
I

AB Title compds. [I; R = (CH2)nZBCOR1; B = bond, CH2, CHMe, CMe2; R1 = cycloalkylidenepiperidino group Q1; A = CH2CH2, CH:CH, CH(OH)CH2, COCH2; X = CH, N; Y = halo- or alkyl-substituted CH:CHCH:CH, SCR2:CH; R2 = H, halo, alkyl; Z = phenylenediyl, thienylenediyl; ZB = indanylenediyl; m = 0, 1; n = 0-2], histamine H, and PAF antagonists (no data), were prepared Thus, I [R = C6H4(CN)-4, m = 0] was hydrolyzed to I [R = C6H4(COR)-4, m = 0] (II; R = OH) which was condensed with benzocycloheptapyridylidenepiperidine Q2H to give II (R = Q2).

IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of histamine H and PAF antagonists)

RN 34580-20-6 CAPLUS

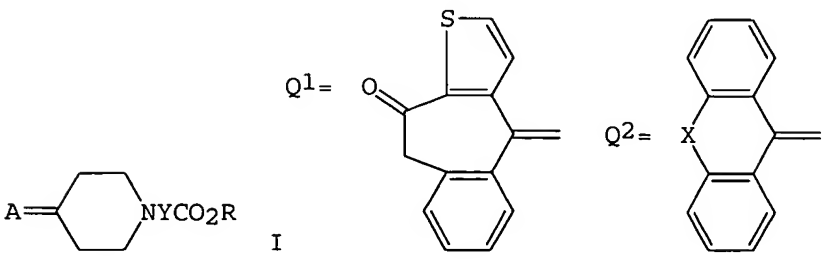
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:83546 CAPLUS
DN 116:83546
TI Preparation of ω-[4-[(hetero)arylidine]piperidino]alkanoates as antiallergic and antihistaminic agents
IN Ito, Yasuo; Kato, Hideo; Koshinaka, Eiichi; Ogawa, Nobuo; Nishino, Hiroyuki; Sakaguchi, Jun
PA Hokuriku Pharmaceutical Co., Ltd., Japan
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 451772	A1	19911016	EP 1991-105567	19910409
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
JP 03294277	A2	19911225	JP 1990-93968	19900411
JP 04001193	A2	19920106	JP 1990-97522	19900416
CA 2038417	AA	19911012	CA 1991-2038417	19910315
PRAI JP 1990-93968	A	19900411		
JP 1990-97522	A	19900416		

OS MARPAT 116:83546
GI



I

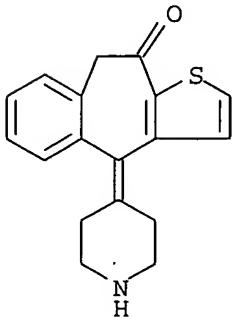
AB Title compds. [I; A = (hetero)arylidene groups Q1, Q2; R = H, alkyl; X = CH2S, S; Y = alkylene] were prepared Thus, 4-(9H-thioxanthen-9-

cyclidene)piperidine (preparation given) was condensed with Br(CH2)3CO2Et to give, after saponification, I (A = Q2, R = H, X = S) [II; Y = (CH2)3]. II (Y = CH2CH2) gave 96% inhibition of passive cutaneous anaphylaxis in rats at 1 mg/kg orally.

IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of antiallergics and antihistaminics)

RN 34580-20-6 CAPLUS

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:216595 CAPLUS

DN 112:216595

TI 4H-Benzo[4,5-cyclohepta[1,2-b]thiophenes and 9,10-dihydro derivatives. Sulfonium analogs of pizotifen and ketotifen. Chirality of ketotifen. Synthesis of the 2-bromo derivative of ketotifen

AU Polivka, Zdenek; Budesinsky, Milos; Holubek, Jiri; Schneider, Bohdan; Sedivy, Zdenek; Svatek, Emil; Matousova, Oluse; Metys, Jan; Valchar, Martin; et al.

CS Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.

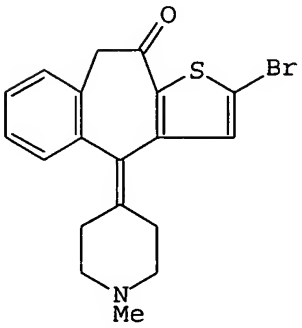
SO Collection of Czechoslovak Chemical Communications (1989), 54(9), 2443-69
CODEN: CCCCAK; ISSN: 0010-0765

DT Journal

LA English

OS CASREACT 112:216595

GI



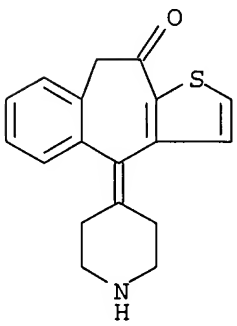
I

AB Sulfonium analogs of pizotifen and ketotifen were prepared The chirality of ketotifen was proven by 1H NMR spectroscopy with the help of the optically active NMR shift reagent. The resolution of racemic ketotifen (I) was achieved by crystallization of salts with optically active O,O'-diacyltartaric acids and homogeneous enantiomers were obtained. The X-ray crystallog. anal. of (+)-I (-)-O,O'-di(p-toluoyl)-(R)-tartrate led to the three-dimensional structure of the mol. of (+)-ketotifen which enabled to determine its absolute configuration to be (R). (R)(+)-ketotifen was found to be the more active ketotifen enantiomer but the stereoselectivity of its action is only a partial one. The 2-bromo derivative of ketotifen, I, was prepared and found to be much less active than ketotifen in the line of antihistamine activity.

IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Me iodide)

RN 34580-20-6 CAPLUS

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:178979 CAPLUS

DN 112:178979

TI Benzo- and pyridocycloheptazoles as platelet activating factor antagonists, antihistamines, and antiinflammatories

IN Friary, Richard J.; Green, Michael J.; Piwinski, John J.

PA Schering Corp., USA

SO Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 339978	A1	19891102	EP 1989-304168	19890426
	EP 339978	B1	19960821		
	R: ES, GR				
	WO 8910363	A1	19891102	WO 1989-US1689	19890426
	W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				

	RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	AU 8935356	A1	19891124	AU 1989-35356	19890426
	AU 631795	B2	19921210		
	ZA 8903103	A	19891227	ZA 1989-3103	19890426
	EP 412988	A1	19910220	EP 1989-905353	19890426
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03504855	T2	19911024	JP 1989-504829	19890426
	JP 2511550	B2	19960626		
	AT 141599	E	19960915	AT 1989-304168	19890426
	ES 2091195	T3	19961101	ES 1989-304168	19890426
	IL 90102	A1	19940731	IL 1989-90102	19890427
	DK 9002569	A	19901217	DK 1990-2569	19901025
	DK 172717	B1	19990614		
	NO 9004666	A	19901227	NO 1990-4666	19901026
	NO 300972	B1	19970825		
	FI 96309	B	19960229	FI 1990-5281	19901026
	FI 96309	C	19960610		
PRAI	US 1988-187105	A	19880428		
	WO 1989-US1689	A	19890426		

OS MARPAT 112:178979

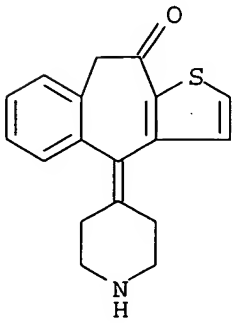
GI For diagram(s), see printed CA Issue.

AB The title compds. [I; K, L = O, (H, alkyl), (H, H), (H, OH), (alkyl, alkyl); when K or L is (H, OH) or O, the other = (H, H), (H, alkyl), (alkyl, alkyl); T = O, Q1; Q = CH, N, NO; U = H, OH, null; W = C, N, NO; X = NCR1(Z), C:NR1(O), NH, etc.; A = atoms to complete (annelated) aromatic 5- or 6-membered rings, e.g. Q2; R1 = H, alkyl, cycloalkyl, CF3, aryl, heteroaryl, amino, alkylthio, alkoxy; R2, R3 = H, alkyl, CF3, NO2, halo, amino, OH, alkoxy, acyloxy, aroyloxy, alkylthio, alkylsulfinyl, alkylsulfonyl; R4 = H, alkyl, aryl], useful as platelet activating factor (PAF) antagonists, antihistamines, and antiinflammatories, were prepared Thus, piperidinylbenzocycloheptathiazole II (no explicit preparation given) at 10 mg/kg orally in guinea pigs gave 38% inhibition of PAF-induced bronchospasm.

IT **34580-20-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, as intermediate for platelet activating factor antagonist)

RN 34580-20-6 CAPLUS

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

10069663

AN 1982:423631 CAPLUS
DN 97:23631
TI Piperidylidene derivatives and pharmaceutical compositions containing them
IN Hasspacher, Klaus
PA Sandoz A.-G., Switz.
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

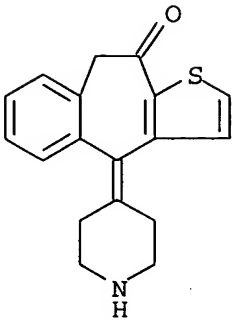
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 47226	A2	19820310	EP 1981-810337	19810819
	EP 47226	A3	19820505		
	EP 47226	B1	19850515		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AT 13297	E	19850615	AT 1981-810337	19810819
	FI 8102635	A	19820303	FI 1981-2635	19810826
	FI 75160	B	19880129		
	FI 75160	C	19880509		
	DK 8103856	A	19820303	DK 1981-3856	19810831
	AU 8174782	A1	19820311	AU 1981-74782	19810831
	AU 547111	B2	19851010		
	CA 1166245	A1	19840424	CA 1981-384939	19810831
	IL 63698	A1	19850630	IL 1981-63698	19810831
	JP 57077673	A2	19820515	JP 1981-138298	19810901
	ES 505106	A1	19830501	ES 1981-505106	19810901
	ZA 8106103	A	19830427	ZA 1981-6103	19810902
	US 4609664	A	19860902	US 1984-631221	19840716
PRAI	CH 1980-6606	A	19800902		
	EP 1981-810337	A	19810819		
	US 1981-296912	A1	19810827		
	US 1983-499371	A1	19830531		

GI For diagram(s), see printed CA Issue.

AB The antiasthmatic title compds. I [X = S, CH2CH2, CH:CH, CH2CO, CH2C(:NOH), CH2CH(OH), X1 = CH:CHCH:CH, SCH:CH, CH:CHCH:N; R = H, acid residue; n = 2, 3] were prepared Thus, 4-(4-piperidylidene)-9-oxo-9,10-dihydro-4H-benzo[4,5]cyclohepta[1,2-b]thiophene was treated with triethylene glycol chlorohydrin to give I (X = CH2CH2, X1 = SCH:CH, R = H, n = 3). The ED50 of I in the passive cutaneous anaphylaxis test was 0.1-3.2 mg/kg.

IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triethylene glycol monochlorohydrin)

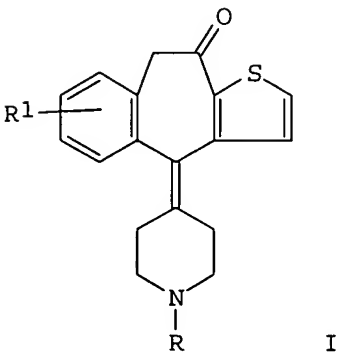
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1976:542973 CAPLUS
DN 85:142973
TI 4-(1-Alkyl-4-piperidylidene)-4H-benzo[4,5]cyclohepta[1,2-b]thiophen-10(9H)-ones and their acid addition salts
PA Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H., Austria
SO Austrian, 9 pp. Division of Austrian 319,238.
CODEN: AUXXAK
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI AT 328445	B	19760325	AT 1973-469	19710310
PRAI AT 1973-469		19710310		

GI

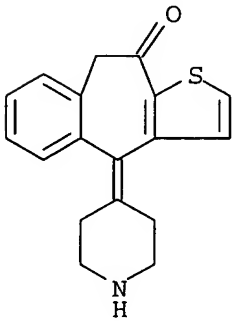


I

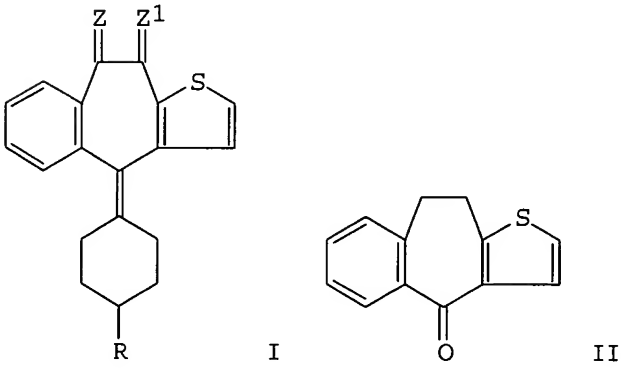
AB Title compds. (I; R = Me, Et, Me2CH, Bu; R1 = H, 6-Br, 6-Cl, 7-Cl, 7-MeO), useful as antihistaminics, are prepared by standard procedures. Thus, reaction of 4-(4-piperidylidene)-4H-benzo[4,5]cyclohepta[1,2-b]thiophen-10(9H)-one, Me2CHI, and Na2CO3 in PhMe for 30 hr at 95° and subsequent treatment with fumaric acid gives the H fumarate of I (R = Me2CH, R1 = H).
IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with isopropyl iodide)
RN 34580-20-6 CAPLUS

10069663

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)

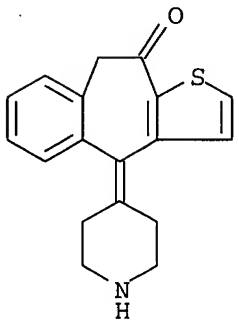


L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1976:446326 CAPLUS
DN 85:46326
TI Studies on synthetic drugs. The 9- and 10-oxo derivatives of 9,10-dihydro-4H-benzo[4,5]-cyclohepta[1,2-b]thiophenes
AU Waldvogel, Erwin; Schwarb, Gustav; Bastian, Jean M.; Bourquin, Jean P.
CS Pharm.-Chem. Forschungslab., Sandoz A.-G., Basel, Switz.
SO Helvetica Chimica Acta (1976), 59(3), 866-77
CODEN: HCACAV; ISSN: 0018-019X
DT Journal
LA German
OS CASREACT 85:46326
GI



AB Benzocycloheptathiophenes I (R = Me, Z = O, Z1 = H2, Z = H2, Z1 = O), antihistaminics (no data), were prepared from II in 6 steps by known methods. I (R = CH2Ph, Z = H2, Z1 = O) (III) was prepared in 3 steps from I (R = Me). III was also converted into its oxide, and into I (R = Me, Z = H,OH, Z1 = H2; Z = H2, Z1 = H,OH; Z = NOH, Z1 = H2; Z = H2, Z1 = NOH; Z = Z1 = O).
IT **34580-20-6P**

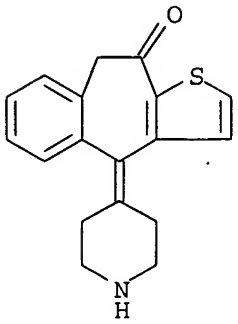
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and benzylation of)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1974:82635 CAPLUS
DN 80:82635
TI Thiophene derivatives
IN Bourquin, Jean P.; Schwarb, Gustav; Waldvogel, Erwin
PA Sandoz Ltd.
SO Patentschrift (Switz.), 4 pp.
CODEN: SWXXAS
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CH 544113	A	19731228	CH 1970-18950	19701222
PRAI CH 1970-18950	A	19701222		

GI For diagram(s), see printed CA Issue.
AB Piperidylidenebenzocycloheptathiophenones I (R = Me2CH, Bu), possessing antihistaminic activity, were prepared by N-alkylating I (R = H) with RX (X = iodo, Br). I (R = H) was prepared by reaction of I (R = Me) and EtO2CCl to give I (R = EtO2C), which was decarbethoxylated with 50% H2SO4BuOH to I (R = H).
IT **34580-20-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 34580-20-6 CAPLUS
CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1973:505088 CAPLUS
DN 79:105088
TI 4-(4-Piperidylidene)-9,10-dihydro-4H-benzo[4,5]cyclohepta[1,2-b]thiophene derivatives
IN Bourquin, Jean P.; Schwarb, Gustav; Waldvogel, Erwin
PA Sandoz Ltd.
SO Ger. Offen., 19 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2302944	A1	19730802	DE 1973-2302944	19730122
	DE 2302944	C2	19821125		
	CH 562244	A	19750530	CH 1972-992	19720124
	CH 565172	A	19750815	CH 1972-988	19720124
	CH 569012	A	19751114	CH 1972-986	19720124
	CH 569006	A	19751114	CH 1972-990	19720124
	US 3862156	A	19750121	US 1972-286281	19720905
	JP 48085575	A2	19731113	JP 1972-117590	19721122
	JP 57060351	B4	19821218		
	DD 102701	C	19731220	DD 1972-167577	19721215
	SE 383347	B	19760308	SE 1973-501	19730115
	DK 134405	B	19761101	DK 1973-225	19730115
	DK 134405	C	19770328		
	FI 55843	C	19791010	FI 1973-110	19730116
	FI 55843	B	19790629		
	NL 7300796	A	19730726	NL 1973-796	19730119
	BE 794377	A1	19730723	BE 1973-126748	19730122
	HU 165130	P	19740628	HU 1973-SA2447	19730122
	GB 1415591	A	19751126	GB 1973-3118	19730122
	PL 83920	P	19760228	PL 1973-160373	19730122
	ES 410856	A1	19760301	ES 1973-410856	19730122
	AT 7300479	A	19760615	AT 1973-479	19730122
	PL 92124	P	19770331	PL 1973-182050	19730122
	AU 7351377	A1	19740725	AU 1973-51377	19730123
	SU 500755	D	19760125	SU 1973-1874899	19730123
	FR 2183663	A2	19731221	FR 1973-2444	19730124
	SU 520914	D	19760705	SU 1974-2017993	19740423
	SU 500761	D	19760125	SU 1974-2027854	19740528
	SU 505364	D	19760228	SU 1974-2027852	19740528

	ES 438598	A1	19770516	ES 1975-438598	19750616
	ES 438596	A1	19770901	ES 1975-438596	19750616
	AT 7506855	A	19761015	AT 1975-6855	19750905
	AT 7506856	A	19761015	AT 1975-6856	19750905
	AT 337181	B	19770610		
	AT 7506857	A	19761015	AT 1975-6857	19750905
	AT 337182	B	19770610		
	SE 7600273	A	19760113	SE 1976-273	19760113
	SE 7600274	A	19760113	SE 1976-274	19760113
	SE 7600275	A	19760113	SE 1976-275	19760113
	SE 423712	B	19820524		
	SE 423712	C	19820902		
	DK 7600161	A	19760115	DK 1976-161	19760115
	DK 7600162	A	19760115	DK 1976-162	19760115
	DK 7600163	A	19760115	DK 1976-163	19760115
	FI 7900145	A	19790117	FI 1979-145	19790117
	FI 59591	B	19810529		
	FI 59591	C	19810910		
	JP 57112390	A2	19820713	JP 1980-175690	19801211
	JP 58017756	B4	19830409		
PRAI	CH 1972-986	A	19720124		
	CH 1972-988	A	19720124		
	CH 1972-990	A	19720124		
	CH 1972-992	A	19720124		
	DK 1973-225	A	19730115		
	FI 1973-110	A	19730116		
	AT 1973-479	A	19730122		

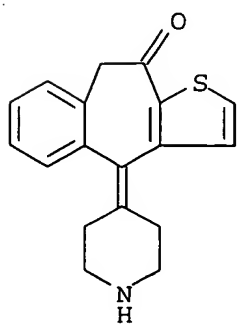
GI For diagram(s), see printed CA Issue.

AB Eight title compds. I, R = Me, Et, CH2Ph, or CH2C6H4Cl-4; X and (or) Y = H2, H and OH, NOH, or O or their hydrochlorides, useful as antihistaminics in the treatment of allergy, were prepared Thus, I (R = Me, X = O, Y = H2) (II) was reduced with NaBH4 in 95% EtOH 3 hr at 20° to give I (R = Me, X = H and OH, Y = H2). Reaction of II with HONH2.HCl in EtOH 1 hr at reflux gave I.HCl (R = Me, X = NOH, Y = H2). Oxidation of I (R = Me, X = H2, Y = O) with SeO2 in AcOH 0.5 hr at reflux gave I (R = Me, X = Y = O). Reaction of I (R = H, X = H2, Y = O) with PhCH2Cl in (Me2N)3PO in the presence of Na2CO3 at 25-50° gave I (R = CH2Ph, X = H2, Y = O).

IT **34580-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with benzyl chloride)

RN 34580-20-6 CAPLUS

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1972:25090 CAPLUS
DN 76:25090
TI 4-(4-Piperidylidene)-4H-benzo[4,5]cyclohepta[1,2-b]thiophenones
IN Bourquin, Jean P.; Schwarb, Gustav; Waldvogel, Erwin
PA Sandoz Ltd.
SO Ger. Offen., 50 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2111071	A	19710923	DE 1971-2111071	19710309
	DE 2111071	C3	19790712		
	DE 2111071	B2	19781109		
	CH 533639	A	19730330	CH 1970-3598	19700311
	CH 531000	A	19730115	CH 1970-531000	19700731
	US 3682930	A	19720808	US 1971-120738	19710303
	RO 61929	B1	19770520	RO 1971-66144	19710304
	SU 422158	D	19740330	SU 1971-1816330	19710305
	SU 512711	D	19760430	SU 1971-1628614	19710305
	FR 2085695	A5	19711231	FR 1971-7901	19710308
	FR 2085695	B1	19741115		
	BE 764019	A1	19710909	BE 1971-100704	19710309
	HU 162868	P	19730428	HU 1971-SA2175	19710309
	ES 389044	A1	19740201	ES 1971-389044	19710309
	IL 36370	A1	19741022	IL 1971-36370	19710309
	PL 84083	P	19760228	PL 1971-146751	19710309
	FI 52980	B	19770930	FI 1971-683	19710309
	CS 185562	P	19781031	CS 1971-1717	19710309
	NL 7103174	A	19710914	NL 1971-3174	19710310
	NL 167431	B	19810716		
	NL 167431	C	19811216		
	DD 100000	C	19730905	DD 1971-164659	19710310
	SE 368954	B	19740729	SE 1971-3074	19710310
	AT 319238	B	19741210	AT 1971-2064	19710310
	CA 960673	A1	19750107	CA 1971-107340	19710310
	AT 319935	B	19750110	AT 1973-470	19710310
	NO 133838	B	19760329	NO 1971-901	19710310
	DK 134404	B	19761101	DK 1971-1114	19710310
	JP 52017030	B4	19770512	JP 1971-13021	19710310
	ZA 7101587	A	19721025	ZA 1971-1587	19710311
	GB 1355537	A	19740605	GB 1971-23482	19710419
	GB 1355538	A	19740605	GB 1973-18940	19710419
	GB 1355539	A	19740605	GB 1973-28823	19710419
	US 3749786	A	19730731	US 1972-278244	19720807
	US 3853915	A	19741210	US 1972-278738	19720808
	CA 966839	A2	19750429	CA 1972-152330	19720922
	ES 416480	A1	19761016	ES 1973-416480	19730630
PRAI	CH 1970-3598	A	19700311		
	CH 1970-11593	A	19700731		
	CH 1970-8598	A	19700311		
	CH 1970-14120	A	19700924		
	CH 1971-1632	A	19710204		
	US 1971-120738	A2	19710303		

CA 1971-107340 A3 19710310
US 1971-178449 19710907
US 1972-278244 19720807

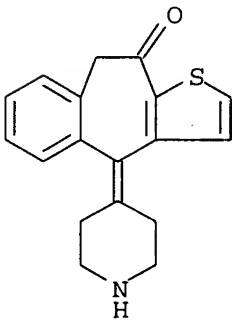
GI For diagram(s), see printed CA Issue.

AB Title compds. (I and II) were prepared by hydrolysis of the corresponding mixture of isomeric enamines or enol ethers and separation by fractional crystallization of their salts. I (R = alkyl) were also prepared by alkylation of I (R = H). Thus, a mixture of 4-(1-methyl-4-piperidylidene)-9-piperidino-4H-benzo[4,5]cyclohepta[1,2-b] thiophene and its 10-piperidino isomer was refluxed 1 hr with 2 N HCl, the mixture made alkaline with concentrated NaOH at 20-5°, and the bases were isolated and separated as fumarates to give I and II (R = Me, R1 = H). To prepare the starting mixture, 9,10-dihydro-4H-benzo[4,5]cyclohepta[1,2-b]thiphen-4-one was brominated with N-bromosuccinimide to give the 9,10-dibromo-9,10-dihydro derivative, which was dehydrobrominated with KOH in MeOH to give the 9 (or 10)-bromo analog, which was reacted with the Grignard compound obtained from 1-methyl-4-chloropiperidine, and the product dehydrated, and treated with piperidine. Similarly prepared were 8 addnl. I, e.g. (R and R1 given): Et, H; Me, 6-Cl; Me, 7-OMe), and the corresponding II.

IT **34580-20-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)

RN 34580-20-6 CAPLUS

CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one, 4,9-dihydro-4-(4-piperidinylidene)- (9CI) (CA INDEX NAME)



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L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2001:208107  CAPLUS
DN   134:242680
TI   Optically active isomers of ketotifen and therapeutically active
     metabolites thereof
IN   Aberg, A. K. Gunnar; Wright, George E.; Chen, Jan L.; Maioli, Andrew T.
PA   Bridge Pharma, Inc., USA
SO   PCT Int. Appl., 27 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2001019367        A1    20010322    WO 2000-US24892         20000912
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             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2383222            AA    20010322    CA 2000-2383222         20000912
     BR 2000013935         A     20020514    BR 2000-13935           20000912
     EP 1218007            A1    20020703    EP 2000-966709          20000912
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
     JP 2003509369         T2    20030311    JP 2001-523001          20000912
PRAI US 1999-153566P       P     19990913
     US 2000-197363P       P     20000415
     US 2000-197905P       P     20000415
     US 2000-197906P       P     20000415
     US 2000-197985P       P     20000415
     WO 2000-US24892       W     20000912
```

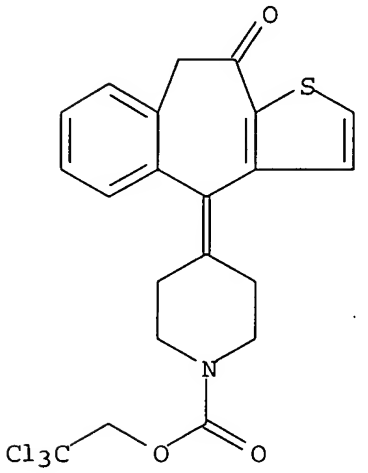
OS MARPAT 134:242680

AB Racemic norketotifen, 10-hydroxy-ketotifen, or 10-hydroxy-nor-ketotifen, and optically active isomers of ketotifen, norketotifen, 10-hydroxy-ketotifen and 10-hydroxy-norketotifen were found to have antiallergic and anti-inflammatory effects while being devoid of the severe dose-limiting sedative side effects of ketotifen. Preparation of R and S isomers of norketotifen as well as their fumarates was presented.

IT **330679-83-9P 330679-84-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antiallergic and anti-inflammatory effects of optically active isomers of ketotifen and therapeutically active metabolites)

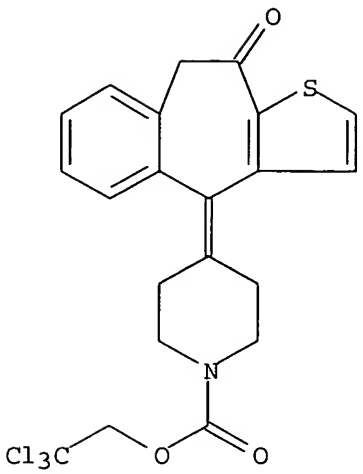
RN 330679-83-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-(9,10-dihydro-10-oxo-4H-benzo[4,5]cyclohepta[1,2-b]thien-4-ylidene)-, 2,2,2-trichloroethyl ester, (4R)- (9CI) (CA INDEX NAME)



RN 330679-84-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-(9,10-dihydro-10-oxo-4H-benzo[4,5]cyclohepta[1,2-b]thien-4-ylidene)-, 2,2,2-trichloroethyl ester, (4S)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT